This listing of claims will replace all prior versions and listing of the claims in the application:

## LISTING OF THE CLAIMS:

Claims 1-53. (canceled)

- Claim 54. (currently amended) A polymcleotide comprising a nucleic acid sequence encoding a polypeptide epitope of a B-cell lymphoma surface immunoglobulin antigen, said polypeptide being useful as a B-cell lymphoma tumor-specific vaccine in a subject with a B-cell lymphoma tumor or at risk of developing a B-cell lymphoma tumor, said polypeptide being encoded at least in part by a nucleic acid in the cells of said B-cell lymphoma tumor, and a nucleic acid sequence promoting expression of said polypeptide in a plant cell or plant and a nucleic acid sequence inducing transient replication of said polypucleotide in the cytoplasm, which polypeptide:
- (a) includes an epitope or epitopes unique to, or overexpressed by, cells of said <u>B-cell lymphoma</u> tumor, thereby distinguishing said <u>B-cell lymphoma</u> tumor from all other tumors (i) of the same or different histological type, (ii) in said subject or in another member of said subject's species; and
  - (b) is formed by two domains linked together by a polypeptide linker;
- $(b \, \underline{c})$  is produced in a plant cell or plant that has been transformed or transfected with said nucleic acid derived from said tumor of said subject;
- (ed) is obtainable from said plant cell or plant in correctly folded form, without a need for denaturation and renaturation and mimics said epitope or epitopes in their native form; and
- (d) is capable of inducing an immune response in a mammal, including said subject, so that administration of said polypeptide results in an antibody or cell-mediated immune response to said epitope or epitopes.

wherein the polypeptide linker:

- (a) has between one and about 50 residues.
- (b) consists of between one and 12 different amino acids, and

- facilitates secretion and correct folding of said polypeptide to mimic the tumor epitope in its native form in or on said tumor cell
- (d) and is a member of a randomized library of linkers that vary in size and sequence, said library is encoded by nucleic acid sequences consisting of a repeated pattern of degenerate repeated triplet nucleotides having the following requirements:
- position 1 of each repeated triplet cannot be the same nucleotide as position 2 of the repeated triplet;
- position 2 of each repeated triplet cannot be the same nucleotide as position 3 of the repeated triplet; or
- (iii) position 1 of each repeated triplet cannot be the same nucleotide as position 3 of the repeated triplet[.]<sub>a</sub>

and

- (iv) position 1 of each repeated triplet is deoxyadenosine or deoxyguanosine;
- (v) position 2 of each repeated triplet is deoxycytidine or deoxyguanosine; and
  - (vi) position 3 of each repeated triplet is deoxythymidine.

## Claim 55. (canceled)

Claim 56. (previously presented) The polynucleotide of claim 54 wherein said polypeptide is produced transiently in said transformed or transfected plant.

## Claims 57-59. (canceled)

Claim 60. (previously presented) The polynucleotide of claim 54 said polypeptide comprising two V region domains of said immunoglobulin.

McCormick et al. Serial No. 09/539,382 Page 4 of 12

Claim 61. (previously presented) The polynucleotide of claim 60 wherein said two domains of said polyneptide are at least part of the  $V_{\rm H}$  and at least part of the  $V_{\rm L}$  domains of said immunoglobulin.

Claim 62. (previously presented) The polynucleotide of claim 61 wherein said part of the  $V_{\rm R}$  region of said polypeptide includes at least one complementarity-determining region (CDR).

Claim 63. (previously presented) The polynucleotide of claim 62 wherein said CDR of said polypeptide is CDR2.

Claim 64. (previously presented) The polynucleotide of claim 61 wherein said polypeptide is a two-domain single-chain antibody (scFV) that includes said at least part of the  $V_{\rm H}$  and  $V_{\rm L}$  domains

Claims 65-71. (canceled)

Claim 72. (previously presented) The polynucleotide of claim 54, wherein said immune response is a protective anti-tumor immune response.

Claim 73. (previously presented) The polynucleotide of claim 54, wherein on administration to a mammalian host, including said subject, said polypeptide induces a polyclonal anti-idiotypic antibody response or a cell mediated immune response.

Claims 74-75. (canceled)

Claim 76. (previously presented) The polynucleotide of claim 73, wherein said administration comprises subcutaneous immunization with at least about 15µg of said polypeptide antigen three times each about two weeks apart.

Claim 77. (currently amended) A polynucleotide encoding a two domain single chain antibody (scFv) wherein a first domain is linked to a second domain by an amino acid linker that

- (ii) has between one and about 50 residues;
- (iii) consists of between one and 12 different amino acids,
- (iv) facilitates secretion and correct folding of said single chain antibody,
- is a member of a randomized library of linkers that vary in size and sequence, and said library is encoded by nucleic acid sequences consisting of a repeated pattern of degenerate repeated triplet nucleotides having the following requirements;
  - a) position 1 of each repeated triplet cannot be the same nucleotide as position 2 of the repeated triplet;
  - position 2 of each repeated triplet cannot be the same nucleotide as position 3 of the repeated triplet; or
  - position 1 of each repeated triplet cannot be the same nucleotide as position 3 of the repeated triplet,

and

- position 1 of each repeated triplet is deoxyadenosine or deoxyguanosine;
- position 2 of each repeated triplet is deoxycytidine or deoxyguanosine; and
- (iii) position 3 of each repeated triplet is deoxythymidine.

## Claim 78. (canceled)

Claim 79. (currently amended) The polynucleotide of claim 77 wherein said scFv includes at least part of the  $V_{\rm H}$  domain and at least part of the  $V_{\rm L}$  domain.

Claim 80. (previously presented) The polynucleotide of claim 79 wherein said domains are those of a surface immunoglobulin epitope of a B-cell lymphoma.

Claim 81. (previously presented) The polynucleotide of claim 54 wherein the polypeptide is capable of inducing said immune response without a need for adjuvant or other immunostimulatory materials.

- Claim 82. (currently amended) A polynucleotide comprising a nucleic acid sequence encoding a polypeptide comprising one or more epitopes of a B-cell lymphoma surface immunoglobulin antigen, said polypeptide being useful as a B-cell lymphoma tumor-specific vaccine in a subject with a B-cell lymphoma tumor or at risk of developing a B-cell lymphoma tumor, encoded at least in part by a nucleic acid in the cells of said tumor, and a nucleic acid sequence of a vector capable of transiently replicating in the cytoplasm of and promoting expression of said polypeptide in a plant cell or plant, which polypeptide:
- (a) includes an one or more epitopes unique to, or overexpressed by, cells of said <u>B-cell lymphoma</u> tumor, thereby distinguishing said <u>B-cell lymphoma</u> tumor from all other tumors (i) of the same or different histological type, (ii) in said subject or in another member of said subject's species;
- (b) is capable of being produced in a plant cell or plant that has been transformed or transfected with said nucleic acid derived from said <u>B-cell lymphoma</u> tumor of said subject;
- (c) is obtainable from said plant cell or plant in correctly folded form, without a need for denaturation and renaturation and mimics said epitope or epitopes in their native form; and
- (d) is capable of inducing an immune response in a manmal, including said subject, so that administration of said polypeptide results in an antibody or cell-mediated immune response to said epitope or epitopes,

wherein the a polypeptide linker which links two domains:

(a) has between one and about 50 residues.

- (b) consists of between one and 12 different amino acids, and
- (c) facilitates secretion and correct folding of said polypeptide to mimic the tumor epitope in its native form in or on said tumor cell
- (d) and is a member of a randomized library of linkers that vary in size and sequence, said library is encoded by nucleic acid sequences consisting of a repeated pattern of degenerate repeated triplet nucleotides having the following requirements:
- (iv) position 1 of each repeated triplet cannot be the same nucleotide as position 2 of the repeated triplet;
- (v) position 2 of each repeated triplet cannot be the same nucleotide as position 3 of the repeated triplet; or
- (vi) position 1 of each repeated triplet cannot be the same nucleotide as position 3 of the repeated triplet.

and

- (iv) position 1 of each repeated triplet is deoxyadenosine or deoxyguanosine;
- (v) position 2 of each repeated triplet is deoxycytidine or deoxyguanosine; and
  - (vi) position 3 of each repeated triplet is deoxythymidine.
- Claim 83. (previously presented) The polynucleotide of claim 82 wherein said vector is a plant virus.
- Claim 84. (previously presented) The polynucleotide of claim 82 wherein said polypeptide is produced transiently in said transformed or transfected plant.
- Claim 85. (previously presented) The polynucleotide of claim 82 wherein said vector contains a subgenomic promoter capable of promoting expression of said polypeptide.

 $\label{eq:claim 86} Claim 86. \quad \text{(previously presented)} \qquad \text{The polynucleotide of claim 82}$  wherein said polypeptide is a two-domain single chain antibody (scFv) that includes said at least part of the VH and the VL domains.

Claim 87. (new) The polynucleotide of claim 54 wherein said polynucleotide is operably linked to a signal sequence that directs newly synthesized protein to a secretory pathway of the plant and said polypeptide obtainable from said plant cell is secreted from said plant cell.

Claim 88. (new) The polynucleotide of claim 77 wherein said polynucleotide is operably linked to a signal sequence that directs newly synthesized protein to a secretory pathway of the plant and said polypeptide obtainable from said plant cell is secreted from said plant cell.

Claim 89. (new) The polynucleotide of claim 82 wherein said polynucleotide is operably linked to a signal sequence that directs newly synthesized protein to a secretory pathway of the plant and said polypeptide obtainable from said plant cell is secreted from said plant cell.